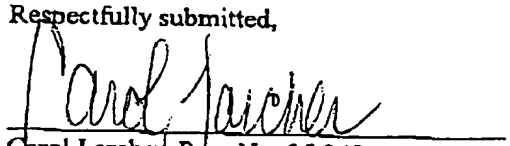
REMARKS

The specification has been amended to insert a cross-reference to related patent applications. The claims have been amended to remove multiple dependencies. No new matter has been added by way of these amendments. Separate documents setting forth the amendments to the specification and claims, as well as all of the pending claims, are attached.

The application is considered to be in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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Date: September 24, 2001

PATENT
Attorney Docket No. 213673

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Beaucage et al.

Art Unit: Unassigned

Application No. Unassigned

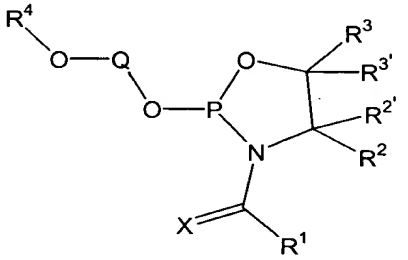
Examiner: Unassigned

Filed: September 24, 2001

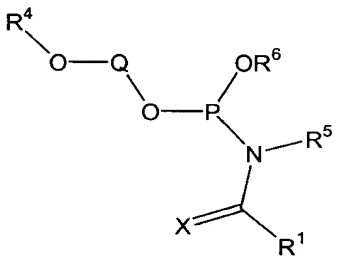
For: N-ACYLPHOSPHORAMIDITES AND THEIR USE IN OLIGONUCLEOTIDE SYNTHESIS

PENDING CLAIMS AFTER ENTRY OF PRELIMINARY AMENDMENT

1. A compound of the formula:



(I) or



(II),

wherein:

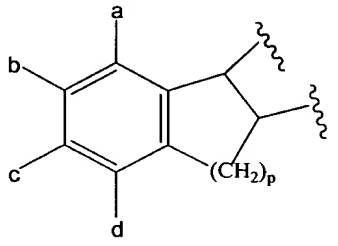
R^1 is an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^1 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of R^7, OR^7, SR^7, NR^8COR^7, NR^8CSR^7, $NR^8CO_2R^7$, $NR^8C(O)SR^7$, $NR^8CS_2R^7$, O_2CR^7, S_2CR^7, $SCOR^7$, $OCSR^7$, SO_2R^7, OSO_2R^7, $NR^8SO_2R^7$, CN, NO_2, N_3, and a halogen, wherein R^7 is an alkyl, an aryl or an aralkyl, wherein R^7 is unsubstituted or substituted with one or more halogen atoms, which are the same or different, and R^8 is H or an alkyl;

R^2 and $R^{2'}$ are the same or different and each is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^2 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of OR^7, CN, NO_2, N_3, and a halogen;

R^3 and $R^{3'}$ are the same or different and each is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^3 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a

trialkylsilyl, an aryldialkylsilyl, an alkyldiarylsilyl, CN, NO_2, N_3, halogens, OR^7, $P(O)(OR^7)(OR^8)$, COR^9, CSR^9, CO_2R^9, $COSR^9$, $CSOR^9$, $CONR^8R^9$, $CSNR^8R^9$, SO_2R^9, and $SO_2NR^8R^9$, wherein R^9 is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, or an aryl, wherein R^9 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of CN, NO_2, N_3, and a halogen; or

R^2 and R^3, $R^{2'}$ and R^3, R^2 and $R^{3'}$, or $R^{2'}$ and $R^{3'}$, together with the carbon atoms to which they are bonded, comprise a cyclic substituent of the formula:



,

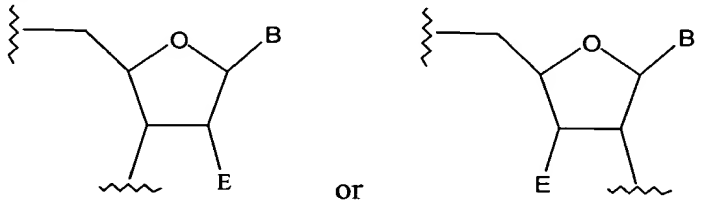
wherein p is an integer from 0-6 and a-d are the same or different and each is selected from the group consisting of H, an alkyl, a nitro, an amino, a hydroxy, a thio, a cyano and a halogen;

R^4 is a protecting group or a solid support;

R^5 is H or an alkyl, which is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of OR^7, CN, NO_2, N_3, and a halogen;

R^6 is a protecting group, an amidoalkyl in which the nitrogen atom is 2, 4, or 5 carbon atoms removed from the oxygen of OR^6, an alkyl, an alkyl ketone, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^6 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of CN, NO_2, N_3, and a halogen;

Q is a nucleoside, an oligonucleotide comprising a nucleoside, or an oligomer comprising a nucleoside, wherein said nucleoside is of the formula:



wherein:

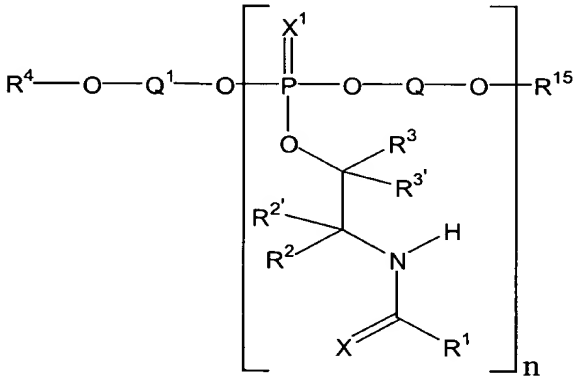
B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the

group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl; and,

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl; and

X is O, S, or Se.

2. A compound of the formula:



(III),

wherein:

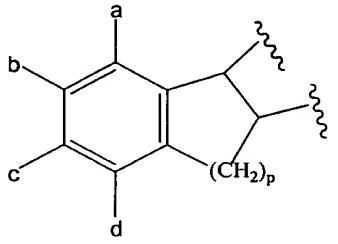
R^1 is an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^1 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of R^7, OR^7, SR^7, NR^8COR^7, NR^8CSR^7, $NR^8CO_2R^7$, $NR^8C(O)SR^7$, $NR^8CS_2R^7$, O_2CR^7, S_2CR^7, $SCOR^7$, $OCSR^7$, SO_2R^7, OSO_2R^7, $NR^8SO_2R^7$, CN, NO_2, N_3, and a halogen, wherein R^7 is an alkyl, an aryl or an aralkyl, wherein R^7 is unsubstituted or substituted with one or more halogen atoms, which are the same or different, and R^8 is H or an alkyl;

R^2 and $R^{2'}$ are the same or different and each is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^2 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of OR^7, CN, NO_2, N_3, and a halogen;

R^3 and $R^{3'}$ are the same or different and each is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^3 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a trialkylsilyl, an aryldialkylsilyl, an alkyldiarylsilyl, CN, NO_2, N_3, a halogen, OR^7, $P(O)(OR^7)(OR^8)$, COR^9, CSR^9, CO_2R^9, $COSR^9$, $CSOR^9$, $CONR^8R^9$, $CSNR^8R^9$, SO_2R^9, and $SO_2NR^8R^9$, wherein R^9 is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, or an

aryl, wherein R^9 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of CN, NO_2, N_3, and a halogen; or

R^2 and R^3, $R^{2'}$ and R^3, R^2 and $R^{3'}$, or $R^{2'}$ and $R^{3'}$, together with the carbon atoms to which they are bonded, comprise a cyclic substituent of the formula:



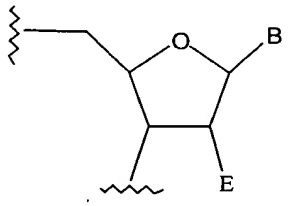
,

wherein p is an integer from 0-6 and a-d are the same or different and each is selected from the group consisting of H, an alkyl, a nitro, an amino, a hydroxy, a thio, a cyano and a halogen;

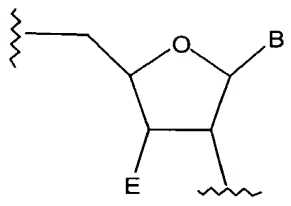
R^4 is a protecting group or a solid support,

R^{15} is H or a protecting group;

Q and Q^1 are the same or different and each is a nucleoside, an oligonucleotide comprising a nucleoside, or an oligomer comprising a nucleoside, wherein said nucleoside is of the formula:



or



wherein:

B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl; and

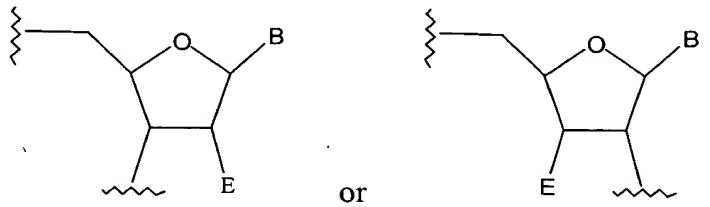
E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl;

X and X^1 are the same or different and each is O, S, or Se; and,

n is an integer from 1 to about 300,

wherein Q is the same or different in each of the units defined by n when n is greater than 1.

3. The compound of claim 1, wherein Q is a nucleoside of the formula:



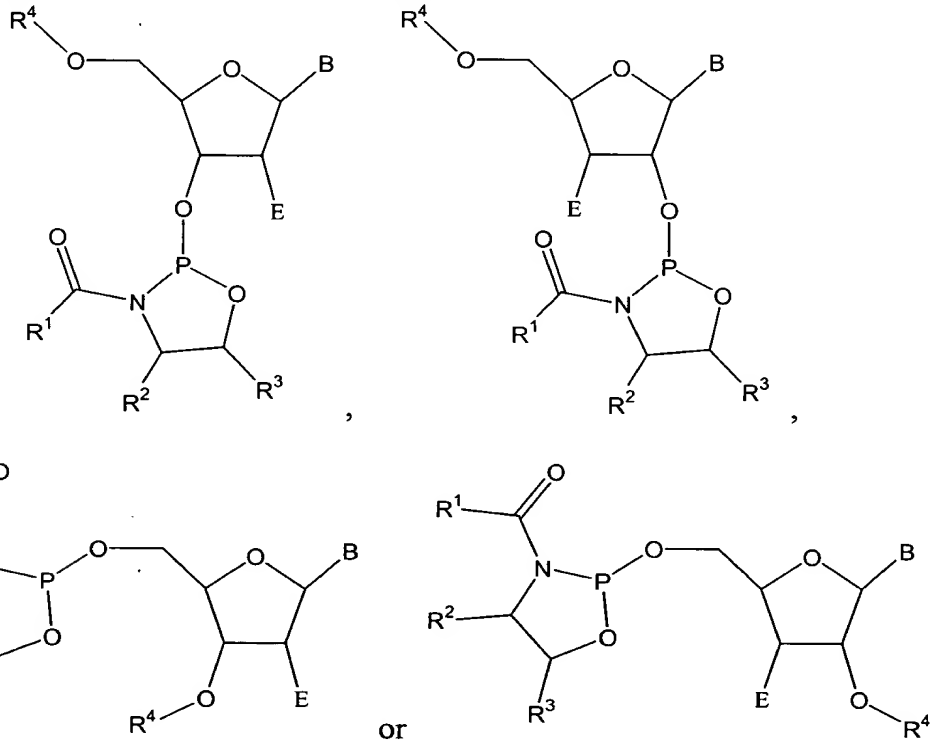
or

wherein:

B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl; and

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl.

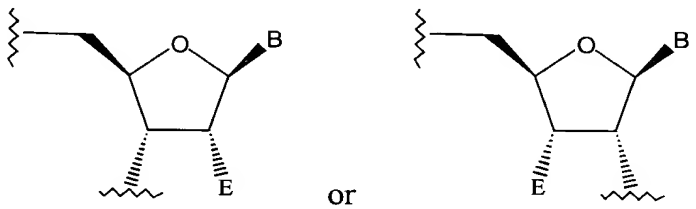
4. The compound of claim 1, wherein said compound is of the formula:



or

wherein R^1-R^4, B, and E are as defined in claim 1.

5. The compound of claim 1, wherein Q is an oligonucleotide comprising a nucleoside, a nucleoside, or an oligomer comprising a nucleoside, wherein said nucleoside is of the formula:



wherein:

B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or a C_1-C_6 alkyl; and

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl.

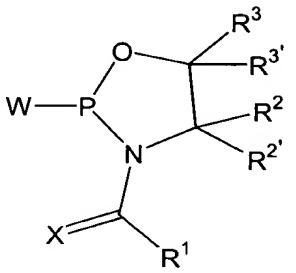
6. The compound of claim 5, wherein B is a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl.

7. The compound of claim 1, wherein R^1 is an alkyl, which is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of fluorine, OR^7, and SR^7, wherein R^7 is an alkyl or an aryl.

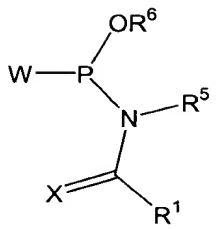
8. The compound of claim 7, wherein R^3 is a vinyl group or a phenyl group.

9. The compound of claim 1, wherein R^4 is a 4,4'-dimethoxytrityl group.

10. A compound of the formula:



(IA), or



(IIA),

wherein:

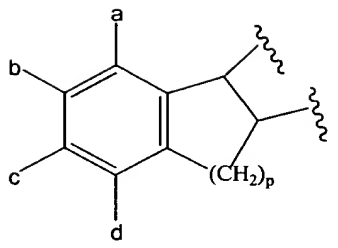
W is a leaving group;

R^1 is an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^1 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of R^7, OR^7, SR^7, NR^8COR^7, NR^8CSR^7, $NR^8CO_2R^7$, $NR^8C(O)SR^7$, $NR^8CS_2R^7$, O_2CR^7, S_2CR^7, $SCOR^7$, $OCSR^7$, SO_2R^7, OSO_2R^7, $NR^8SO_2R^7$, CN, NO_2, N_3, and a halogen, wherein R^7 is an alkyl, an aryl or an aralkyl, wherein R^7 is unsubstituted or substituted with one or more halogen atoms, which are the same or different, and R^8 is H or an alkyl;

R^2 and $R^{2'}$ are the same or different and each is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^2 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of OR^7, CN, NO_2, N_3, and a halogen;

R^3 and $R^{3'}$ are the same or different and each is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^3 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a trialkylsilyl, an aryldialkylsilyl, an alkyldiarylsilyl, CN, NO_2, N_3, a halogen, OR^7, $P(O)(OR^7)(OR^8)$, COR^9, CSR^9, CO_2R^9, $COSR^9$, $CSOR^9$, $CONR^8R^9$, $CSNR^8R^9$, SO_2R^9, and $SO_2NR^8R^9$, wherein R^9 is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, or an aryl, wherein R^9 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of CN, NO_2, N_3, and a halogen; or

R^2 and R^3, $R^{2'}$ and R^3, R^2 and $R^{3'}$, or $R^{2'}$ and $R^{3'}$, together with the carbon atoms to which they are bonded, comprise a cyclic substituent of the formula:



,

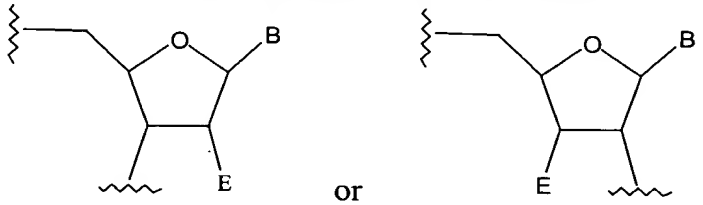
wherein p is an integer from 0-6 and a-d are the same or different and each is selected from the group consisting of H, an alkyl, a nitro, an amino, a hydroxy, a thio, a cyano and a halogen;

R^4 is a protecting group or a solid support;

R^5 is H or an alkyl, which is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of OR^7, CN, NO_2, N_3, and a halogen;

R^6 is a protecting group, an amidoalkyl in which the nitrogen atom thereof is 2, 4, or 5 carbon atoms removed from the oxygen of OR^6, an alkyl, an alkyl ketone, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^6 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of CN, NO_2, N_3, and a halogen;

Q is an a nucleoside, oligonucleotide comprising a nucleoside, or an oligomer comprising a nucleoside, wherein said nucleoside is of the formula:



wherein:

B is a labeling group, an alkyl, an alkenyl an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl; and,

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl; and

X is O, S, or Se.

11. The compound of claim 10, wherein W is halogen, a dialkylamino having from 2 to about 8 carbon atoms, or a cyclic amine having from 2 to about 6 carbon atoms, wherein one or more carbon atoms of the dialkylamino or cyclic amine are optionally substituted with one or more heteroatoms, which are the same or different.

12. A method of preparing a polymer, said method comprising the steps of:

(a) reacting a nucleophile that can displace the N-acyl group of an N-acylphosphoramidite with the N-acylphosphoramidite of claim 1, wherein R^4 is a protecting group, to produce an adduct of said N-acylphosphoramidite and said nucleophile, said adduct comprising a tricoordinated phosphorus atom;

(b) reacting said adduct with a reagent selected from the group consisting of oxidizing agents, sulfurizing agents, and selenizing agents, to produce a product, wherein said tricoordinated phosphorus atom is converted into a phosphorus atom with a valence of greater than three;

(c) removing the protecting group R^4 from the product; and

(d) optionally repeating steps (a) through (c) one or more times until a polymer of specified length is obtained.

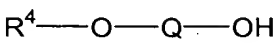
13. The method of claim 12, further comprising the step of cleaving the bond linking the organic moiety to the non-bridging phosphate, phosphorothioate or phosphoroselenoate oxygen atom in the product obtained in step (c) or (d).

14. The method of claim 13, wherein the bond linking the organic moiety to the non-bridging phosphate, phosphorothioate or phosphoroselenoate oxygen atom is cleaved chemically.

15. The method of claim 13, wherein the bond linking the organic moiety to the non-bridging phosphate, phosphorothioate or phosphoroselenoate oxygen atom is cleaved thermally.

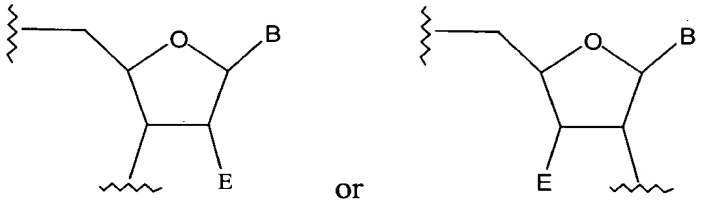
16. The method of claim 12, wherein said nucleophile is attached to a solid support.

17. The method of claim 12, wherein said nucleophile is of the formula:



wherein:

Q is a nucleoside, oligonucleotide comprising a nucleoside, or an oligomer comprising a nucleoside, wherein said nucleoside is of the formula:



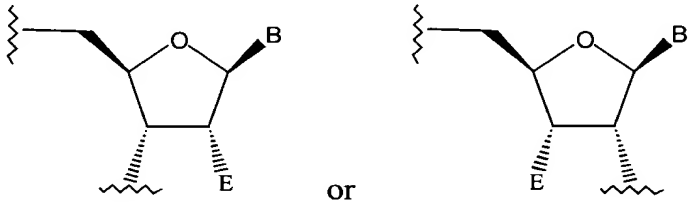
wherein:

B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl; and

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl; and

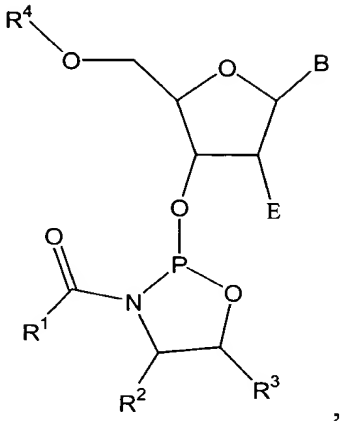
R^4 is a solid support.

19. The method of claim 17, wherein Q is a nucleoside, an oligonucleotide comprising a nucleoside, or an oligomer comprising a nucleoside, wherein said nucleoside is of the formula:



wherein B and E are as defined in claim 17.

20. The method of claim 12, wherein said N-acylphosphoramidite is of the formula: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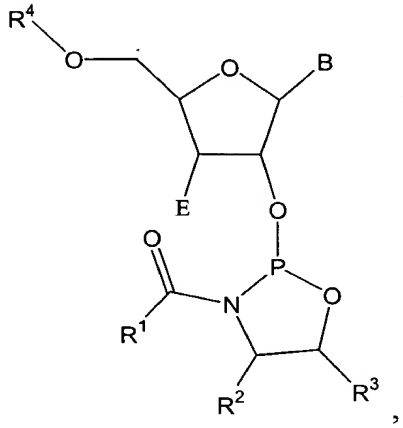
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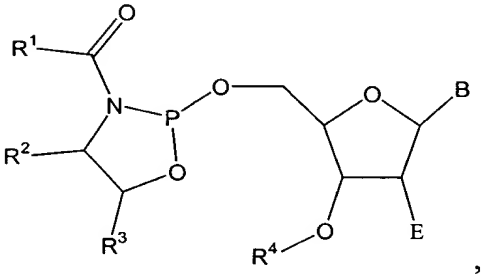
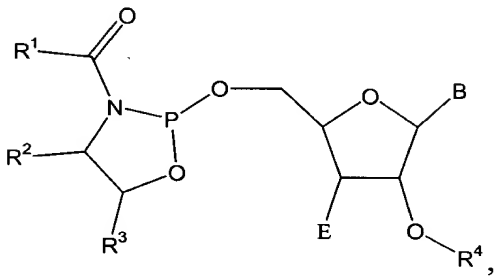

, or


,

wherein:

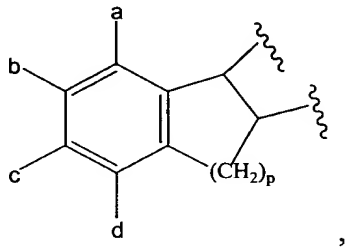
R^1 is an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^1 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of R^7, OR^7, SR^7, NR^8COR^7, NR^8CSR^7, $NR^8CO_2R^7$, $NR^8C(O)SR^7$, $NR^8CS_2R^7$, O_2CR^7, S_2CR^7, $SCOR^7$, $OCSR^7$, SO_2R^7, OSO_2R^7, $NR^8SO_2R^7$, CN, NO_2, N_3, and a halogen, wherein R^7 is an alkyl, an aryl or an aralkyl, wherein R^7 is unsubstituted or substituted with one or more halogen atoms, which are the same or different, and R^8 is H or an alkyl;

R^2 is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^2 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of OR^7, CN, NO_2, N_3, and a halogen;

R^3 is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^3 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a trialkylsilyl, an aryldialkylsilyl, an alkyldiarylsilyl, CN, NO_2, N_3, a halogen, OR^7, $P(O)(OR^7)(OR^8)$, COR^9, CSR^9, CO_2R^9, $COSR^9$, $CSOR^9$, $CONR^8R^9$, $CSNR^8R^9$, SO_2R^9, and $SO_2NR^8R^9$, wherein R^9 is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, or an aryl, wherein R^9 is unsubstituted or

substituted with one or more substituents, which are the same or different, selected from the group consisting of CN, NO_2, N_3, and a halogen; or

R^2 and R^3, together with the carbon atoms to which they are bonded, comprise a cyclic substituent of the formula:



,

wherein p is an integer from 0-6 and a-d are the same or different and each is selected from the group consisting of H, an alkyl, a nitro, an amino, a hydroxy, a thio, a cyano and a halogen;

R^4 is a protecting group or a solid support;

B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl; and,

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl.

21. The method of claim 20, wherein B is a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl.

22. The method of claim 20, wherein R^1 is an alkyl, which is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of fluorine, OR^7, and SR^7, wherein R^7 is an alkyl, an aryl, or an aralkyl.

23. The method of claim 20, wherein R^3 is a vinyl group, a phenyl, or a benzyl.

24. The method of claim 20, wherein R^4 is a 4,4'-dimethoxytrityl group.

25. A method of synthesizing an oligomer or polymer, said method comprising:

(i) providing a nucleophile;

(ii) reacting said nucleophile, in the presence of a mild acid, with the compound of claim 10 or 11, to produce an adduct;

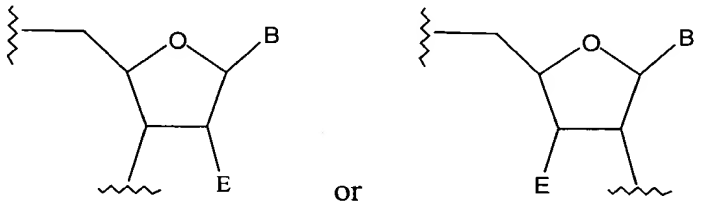
(iii) reacting the resulting product, in the presence of a base, with a nucleoside, having at least one nucleophilic group and at least one suitably protected nucleophilic group, to produce a product;

(iv) deprotecting the protected nucleophilic group of the resulting product;

(v) oxidatively transforming the tricoordinated phosphorus atom into a tetracoordinated one; and

(vi) repeating the steps (ii)-(v) until an oligomer or polymer of predetermined length is obtained.

26. The compound of claim 2, wherein each of Q and Q^1 is a nucleoside of the formula:



wherein:

Q and Q^1 are the same or different;

B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl; and

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl.

27. The compound of claim 2, wherein R^1 is an alkyl, which is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of fluorine, OR^7, and SR^7, wherein R^7 is an alkyl or an aryl.

28. The compound of claim 2, wherein R^4 is a 4,4'-dimethoxytrityl group.

PATENT
Attorney Docket No. 213673

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Beaucage et al.

Application No. Unassigned

Filed: September 24, 2001

Art Unit: Unassigned

Examiner: Unassigned

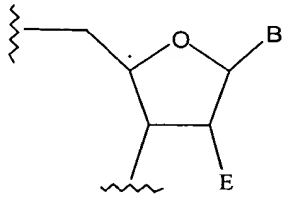
For: N-ACYLPHOSPHORAMIDITES AND THEIR USE IN OLIGONUCLEOTIDE SYNTHESIS

AMENDMENTS TO CLAIMS
MADE VIA PRELIMINARY AMENDMENT

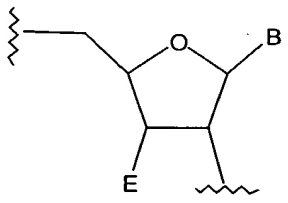
Claim 18 has been deleted.

The following claims have been amended:

3. (Amended) The compound of claim 1 [or 2], wherein [each of]Q [and Q^1] is a nucleoside of the formula:



or



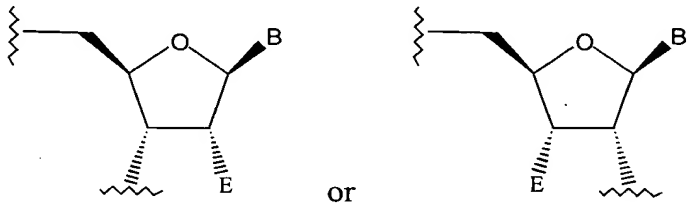
wherein:

[in the compound of claim 2, Q and Q' are the same or different;]

B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl; and

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl.

5. (Amended) The compound of [any of claims 1, 2, or 4] claim 1, wherein [each of] Q [and Q^1] is an oligonucleotide comprising a nucleoside, a nucleoside, or an oligomer comprising a nucleoside, wherein said nucleoside is of the formula:



wherein:

[in the compound of claim 2, Q and Q' are the same or different;]

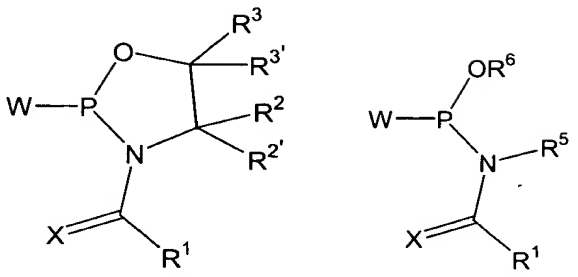
B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or a C_1-C_6 alkyl; and

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl.

7. (Amended) The compound of [any of claims 1, 2, 4, or 6] claim 1, wherein R^1 is an alkyl, which is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of fluorine, OR^7, and SR^7, wherein R^7 is an alkyl or an aryl.

9. (Amended) The compound of [any of claims 1, 2, 4, 6 or 8] claim 1, wherein R^4 is a 4,4'-dimethoxytrityl group.

10. (Amended) A compound of the formula:



[(IA), (IIA),]

(IA), or (IIA),

wherein:

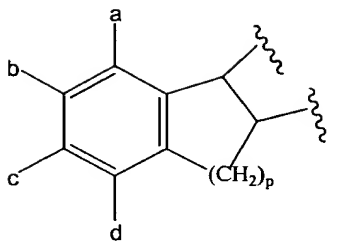
W is a leaving group;

R^1 is an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^1 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of R^7, OR^7, SR^7, NR^8COR^7, NR^8CSR^7, $NR^8CO_2R^7$, $NR^8C(O)SR^7$, $NR^8CS_2R^7$, O_2CR^7, S_2CR^7, $SCOR^7$, $OCSR^7$, SO_2R^7, OSO_2R^7, $NR^8SO_2R^7$, CN, NO_2, N_3, and a halogen, wherein R^7 is an alkyl, an aryl or an aralkyl, wherein R^7 is unsubstituted or substituted with one or more halogen atoms, which are the same or different, and R^8 is H or an alkyl;

R^2 and $R^{2'}$ are the same or different and each is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^2 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of OR^7, CN, NO_2, N_3, and a halogen;

R^3 and $R^{3'}$ are the same or different and each is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^3 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a trialkylsilyl, an aryldialkylsilyl, an alkyldiarylsilyl, CN, NO_2, N_3, a halogen, OR^7, $P(O)(OR^7)(OR^8)$, COR^9, CSR^9, CO_2R^9, $COSR^9$, $CSOR^9$, $CONR^8R^9$, $CSNR^8R^9$, SO_2R^9, and $SO_2NR^8R^9$, wherein R^9 is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, or an aryl, wherein R^9 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of CN, NO_2, N_3, and a halogen; or

R^2 and R^3, $R^{2'}$ and R^3, R^2 and $R^{3'}$, or $R^{2'}$ and $R^{3'}$, together with the carbon atoms to which they are bonded, comprise a cyclic substituent of the formula:



,

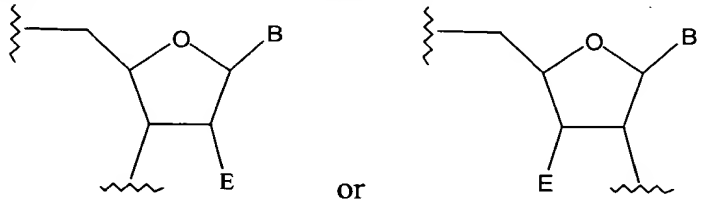
wherein p is an integer from 0-6 and a-d are the same or different and each is selected from the group consisting of H, an alkyl, a nitro, an amino, a hydroxy, a thio, a cyano and a halogen;

R^4 is a protecting group or a solid support;

R^5 is H or an alkyl, which is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of OR^7, CN, NO_2, N_3, and a halogen;

R^6 is a protecting group, an amidoalkyl in which the nitrogen atom thereof is 2, 4, or 5 carbon atoms removed from the oxygen of OR^6, an alkyl, an alkyl ketone, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^6 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of CN, NO_2, N_3, and a halogen;

Q is an a nucleoside, oligonucleotide comprising a nucleoside, or an oligomer comprising a nucleoside, wherein said nucleoside is of the formula:



wherein:

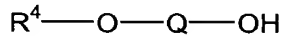
B is a labeling group, an alkyl, an alkenyl an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl; and,

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl; and

X is O, S, or Se.

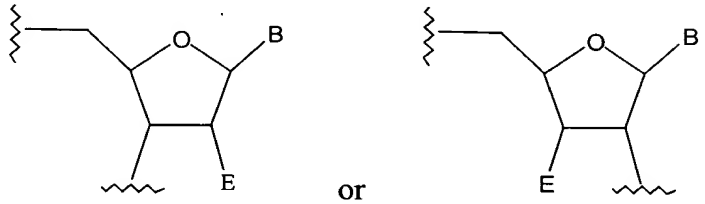
16. (Amended) The method of [any of claims 12-15] claim 12, wherein said nucleophile is attached to a solid support.

17. (Amended) The method of claim [16] 12, wherein said nucleophile is of the formula:



wherein:

Q is a nucleoside, oligonucleotide comprising a nucleoside, or an oligomer comprising a nucleoside, wherein said nucleoside is of the formula:



or

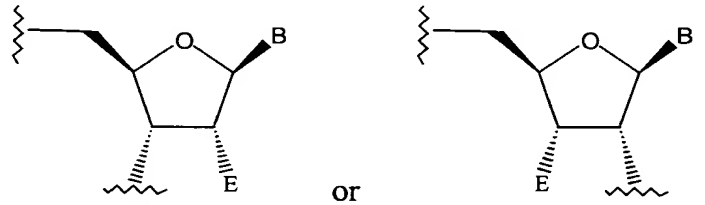
wherein:

B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl; and

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl; and

R^4 is a solid support.

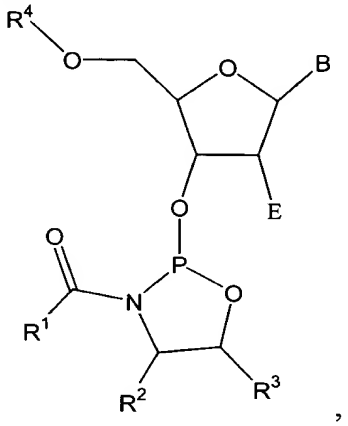
19. (Amended) The method of claim [14] 17, wherein Q is a nucleoside, an oligonucleotide comprising a nucleoside, or an oligomer comprising a nucleoside, wherein said nucleoside is of the formula:



or

wherein B and E are as defined in claim [14]17.

20. (Amended) The method of [any of claims 12-15 or 17-19] claim 12, wherein said N-acylphosphoramidite is of the formula: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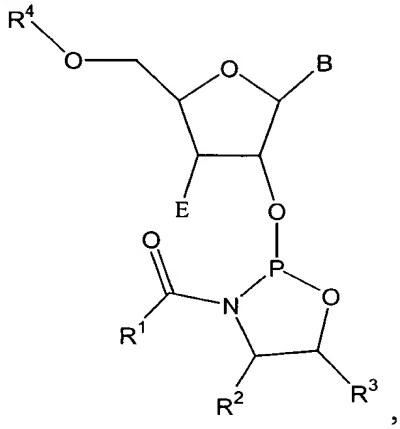
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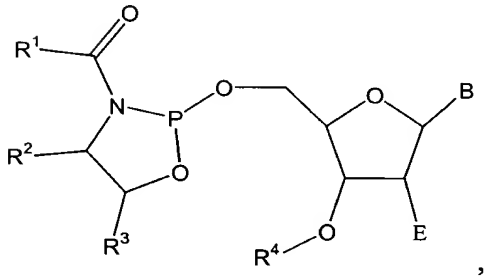
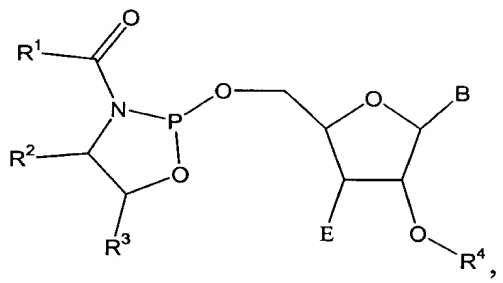

, or

,

wherein:

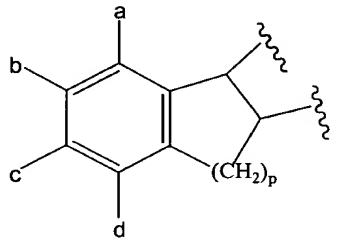
R^1 is an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^1 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of R^7, OR^7, SR^7, NR^8COR^7, NR^8CSR^7, $NR^8CO_2R^7$, $NR^8C(O)SR^7$, $NR^8CS_2R^7$, O_2CR^7, S_2CR^7, $SCOR^7$, $OCSR^7$, SO_2R^7, OSO_2R^7, $NR^8SO_2R^7$, CN, NO_2, N_3, and a halogen, wherein R^7 is an alkyl, an aryl or an aralkyl, wherein R^7 is unsubstituted or substituted with one or more halogen atoms, which are the same or different, and R^8 is H or an alkyl;

R^2 is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^2 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of OR^7, CN, NO_2, N_3, and a halogen;

R^3 is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, or an aralkyl, wherein R^3 is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a trialkylsilyl, an aryldialkylsilyl, an alkyldiarylsilyl, CN, NO_2, N_3, a halogen, OR^7, $P(O)(OR^7)(OR^8)$, COR^9, CSR^9, CO_2R^9, $COSR^9$, $CSOR^9$, $CONR^8R^9$, $CSNR^8R^9$, SO_2R^9, and $SO_2NR^8R^9$, wherein R^9 is H, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aralkyl, or an aryl, wherein R^9 is unsubstituted or

substituted with one or more substituents, which are the same or different, selected from the group consisting of CN, NO_2, N_3, and a halogen; or

R^2 and R^3, together with the carbon atoms to which they are bonded, comprise a cyclic substituent of the formula:



,

wherein p is an integer from 0-6 and a-d are the same or different and each is selected from the group consisting of H, an alkyl, a nitro, an amino, a hydroxy, a thio, a cyano and a halogen;

R^4 is a protecting group or a solid support;

B is a labeling group, an alkyl, an alkenyl, an alkynyl, a cycloalkyl, an aryl, a heteroaryl, a heterocycloalkyl, an aralkyl, an amino, an alkylamino, a dialkylamino, a purine, a pyrimidine, adenine, guanine, cytosine, uracil, or thymine, wherein B is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of a protecting group, R^{11}, OR^{11}, NHR^{11}, $NR^{11}R^{12}$, CN, NO_2, N_3, and a halogen, wherein R^{11} and R^{12} are the same or different and each is H, a protecting group, or an alkyl; and,

E is H, a halogen, OR^{13}, NHR^{13}, or $NR^{13}R^{14}$, wherein R^{13} and R^{14} are the same or different and each is H, a protecting group, an alkyl, or an acyl.

22. (Amended) The method of [any of claims 12-15, 17-19 or 21] claim 20, wherein R^1 is an alkyl, which is unsubstituted or substituted with one or more substituents, which are the same or different, selected from the group consisting of fluorine, OR^7, and SR^7, wherein R^7 is an alkyl, an aryl, or an aralkyl.

23. (Amended) The method of claim [22] 20, wherein R^3 is a vinyl group, a phenyl, or a benzyl.

24. (Amended) The method of [any of claims 12-15, 17-19, 21 or 23] claim 20, wherein R^4 is a 4,4'-dimethoxytrityl group.